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RAPID COMMUNICATION

Category-Sensitive Excitatory and Inhibitory Processes in Human Extrastriate Cortex

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Allison, Truett, Aina Puce, and Gregory McCarthy. Category-sensitive excitatory and inhibitory processes in human extrastriate cortex. *J Neurophysiol* 88: 2864–2868, 2002; 10.1152/jn.00202.2002. Single-cell recordings from the temporal lobe of monkeys viewing stimuli show that cells may be highly selective, responding for example to particular objects such as faces. However, stimulus-selective cells may be inhibited by nonpreferred stimuli. Can such inhibitory mechanisms be detected in human visual cortex? In previous recordings from the surface of human ventral extrastriate cortex, we found that specific categories of stimuli such as faces and words generate category-specific negative event-related potentials (ERPs) with a peak latency of about 200 ms (N200). Laminar recordings in animal cortex suggest that the human N200 reflects excitatory depolarizing potentials in apical dendrites of pyramidal cells. In this study we found that, at about half of word-specific N200 sites, faces generated a positive ERP (P200); conversely, at about half of face-specific sites, words generated P200s. The electrogenesis of N200 implies that P200 ERPs reflect hyperpolarizing inhibition of apical dendrites. These recordings, together with the prior animal recordings, provide strong circumstantial evidence that in human cortex populations of cells responsive to one stimulus category (such as faces) inhibit cells responsive to another category (such as words), probably by a type of lateral inhibition. Of the stimulus categories studied quantitatively, face-specific cells are maximally inhibited by words and vice versa, but other categories of stimuli may generate smaller P200s, suggesting that inhibition of category-specific cells by nonpreferred stimuli is a general feature of human extrastriate cortex involved in object recognition.

INTRODUCTION

Single-cell recordings from the temporal lobe of monkeys viewing complex stimuli show that cells may be highly selective, responding for example to complex nonobjects (e.g., Fujita et al. 1992) or to objects such as faces (reviewed by Desimone 1991; Perrett et al. 1992) and hands (Gross et al. 1969). Conversely, stimulus-selective cells may be inhibited by nonpreferred stimuli (Baylis et al. 1985; Perrett et al. 1991; Tamura and Tanaka 2001). Part of the specificity of such cells results from local inhibitory interactions. For example, decreases in stimulus specificity can occur from blockade of inhibition by local injection of bicuculline (Wang et al. 2000).

Such inhibitory mechanisms presumably exist in human ventral extrastriate cortex, but single-cell recordings cannot be obtained in this inaccessible region. In this study, inhibitory interactions were inferred from event-related potential (ERP) recordings made directly from the surface of the fusiform gyrus and adjacent cortex, regions known from neurophysiological and neuroimaging studies to be involved in the perception of faces, objects, and words (reviewed by Haxby et al. 2000; McCarthy 1999; Polk et al. 2002; Puce et al. 1999). A preliminary report of these results has appeared (Allison et al. 2001).

METHODS

ERP recordings pertinent to this study were obtained from 34 patients in whom face-specific and/or word-specific N200 ERPs (Allison et al. 1999) were recorded. These recordings contained the following stimulus categories: human faces (gray-scale front views), phase-scrambled faces, words (common concrete nouns, white on a dark background), phase-scrambled words, and living things (gray-scale flowers). (Recordings with other stimulus categories yielded results similar to those reported here but did not have enough categories in common to allow quantitative analysis.) The patients had medically intractable epilepsy and were being evaluated for possible surgery (Spencer et al. 1990). They viewed 500-ms duration images (presented randomly at 1.8–2.2 s intervals) while a 64- or 128-channel electrocorticogram (filtered at 0.1–100 Hz, digitized at 250 Hz, with mastoids serving as reference and ground) was recorded simultaneously from 2.2-mm-diam subdural electrodes; for details see Allison et al. (1999). Informed consent was obtained using protocols approved by the Human Investigation Committee of Yale Medical School.

RESULTS

Recordings made from the inferior surface of occipitotemporal cortex reveal several patterns of responsivity. Most electrodes in this region record no, or small undifferentiated, ERPs to all categories of stimuli. At approximately 25% of sites that generated a category-specific N200, other categories of stimuli generated small N200s, suggesting that the active cells were responsive primarily to the preferred stimulus (faces in the example of Fig. 1*A*) but were also slightly responsive to other

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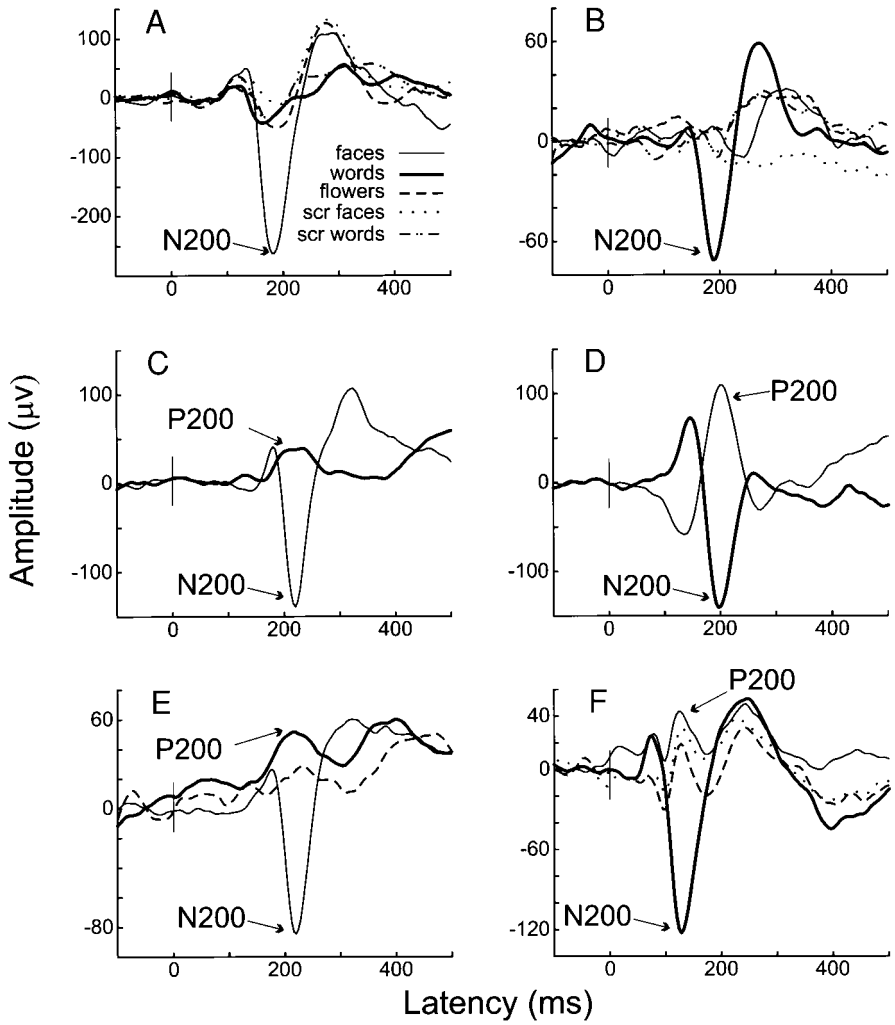

FIG. 1. *A*: at this face-specific N200 site, other categories of stimuli generated small N200s. *B*: at this word-specific N200 site, other categories of stimuli generated no clear event-related potentials (ERPs) in the latency range of N200. *C*: example of an N200 evoked by faces and a P200 evoked by words at a face-specific N200 site. *D*: example of an N200 evoked by words and a P200 evoked by faces at a word-specific N200 site. *E*: at this face-specific N200 site, words and flowers evoked P200s. *F*: at this word-specific N200 site faces, scrambled faces and flowers evoked P200s. Positive plotted upward, stimulus onset at 0 ms, line types illustrated in *A* apply to entire figure.

categories of stimuli. At other category-specific N200 sites (approximately 25% of the total), preferred stimuli (words in the example of Fig. 1*B*) evoked an N200, whereas nonpreferred stimuli evoked little or no measurable activity in the latency range of N200, suggesting that the active cells responded only to preferred stimuli.

For the purposes of this paper, another pattern of responsivity, observed at approximately half of category-specific sites, is illustrated in Fig. 1,*C–F*. At the face-specific site of Fig. 1*C*, words evoked a positive ERP (P200) at approximately the same latency as the N200 evoked by faces. Similarly, at a word-specific N200 site (Fig. 1*D*), faces evoked a P200. This phenomenon was most obvious for the stimulus categories of faces and words, but P200s were sometimes evoked (although usually smaller in amplitude) by other categories of stimuli (Fig. 1, *E* and *F*). A total of 20 face-specific N200 sites with associated P200s and 15 word-specific N200 sites with associated P200s, were found.

The peak latency of each P200 is plotted against its corresponding N200 latency in Fig. 2*A*. P200 latency was closely related to N200 latency at both face- and word-specific sites. P200 amplitudes, relative to their corresponding N200 amplitudes, are plotted in Fig. 2*B*. At face-specific sites, words evoked P200s that were on average 34% as large as N200. At word-specific sites, faces evoked P200s that were on average 62% as large as N200. Although the largest P200s were evoked by words and faces, smaller P200s were sometimes evoked by objects such as flowers and by scrambled faces or words (Fig. 2*B*). Face- and word-specific N200 sites were on the fusiform, inferior temporal, and inferior occipital gyri (Fig. 2*D*), typical of the sites reported in a larger study of category-specific N200s (Allison et al. 1999).

DISCUSSION

This study demonstrates that patches of human extrastriate cortex that generate N200 ERPs to preferred stimuli often generate P200 ERPs to nonpreferred stimuli. What is the electrophysiological basis of these two types of ERPs and what functionality do they imply? The initial negativity generated in primary sensory cortex by an afferent stimulus—referred to as the primary negativity in the older literature (see for example Towe 1966)—is thought to reflect the excitatory depolarization of apical dendrites of pyramidal cells (reviewed by Creutzfeldt and Houchin 1974; Schlag 1973; Wood and Allison 1981). Recent current source density analysis in monkey visual cortex supports the older conclusion by demonstrating current sinks in apical dendrites after visual stimulation (Mehta et al. 2000). The apical dendritic depolarization recorded here as N200 is

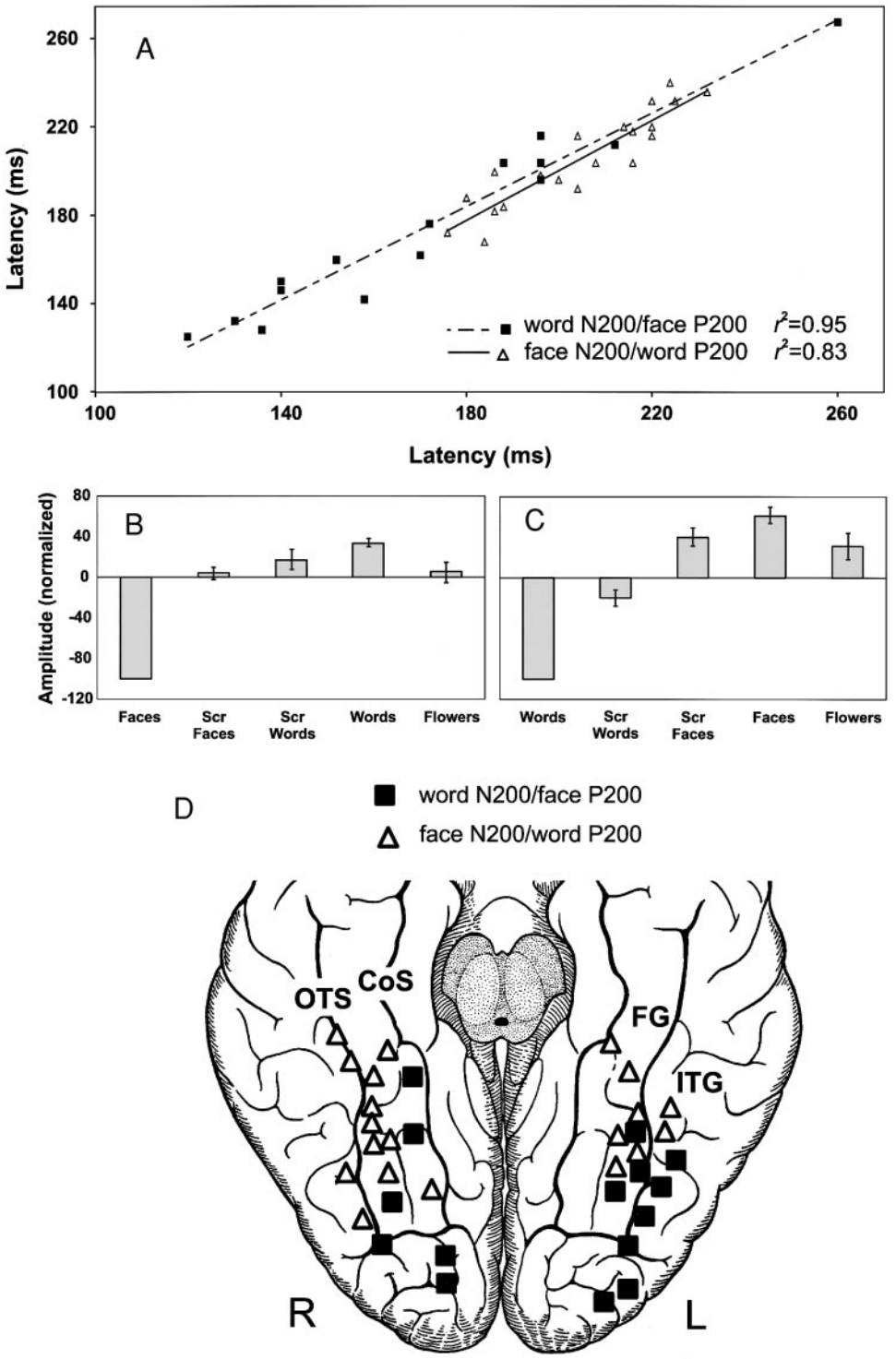

FIG. 2. *A*: peak latency of face-specific N200s and word P200s (△), and word-specific N200s and face P200s (■). P200 amplitudes (±SE) to categories of stimuli at face-specific (*B*) and at word-specific (*C*) sites, calculated relative to prestimulus baseline. Amplitudes normalized to category-specific N200 amplitude = −100. *D*: N200/P200 recording sites shown on an inferior view (cerebellum removed, brain anterior to the optic chiasm not shown) of a representative brain. Locations were determined from magnetic resonance images (MRIs) obtained after electrode implantation. CoS, collateral sulcus; FG, fusiform gyrus; ITG, inferior temporal gyrus; OTS, occipitotemporal sulcus. For face-specific N200 sites ($n = 20$), the center of activation in Talairach coordinates was $x = |41|$, $y = -56$; for word-specific N200 sites ($n = 15$) the corresponding values were $x = |32|$, $y = -72$.

evoked either by direct synaptic activation of dendrites or by backpropagation from the soma (Stuart et al. 1997).

If this conclusion is correct, then it follows that P200 likely reflects hyperpolarizing inhibition of the same population of apical dendrites and hence reflects a modulatory inhibition of cells that prefer a particular category of stimuli (such as faces) by another population of cells that prefer a different category of stimuli (such as words). This model of electrogenesis is illustrated schematically in Fig. 3. The simplest mechanism of inhibition consistent with the data is a recurrent collateral inhibition, as illustrated in Fig. 3, but any lateral inhibitory process that induced a hyperpolarization of apical dendrites would, according to this model, be equally effective. Excitatory and inhibitory postsynaptic potentials (EPSPs and IPSPs) are known to be generated in apical dendrites of pyramidal cells, but the sources of these excitatory and inhibitory inputs have not been specifically identified (reviewed by Rockland 1998). The peak latency of a P200 was highly correlated with, and similar to, its corresponding N200 latency (Fig. 2*A*), suggesting that the inhibition is a relatively local process. In this

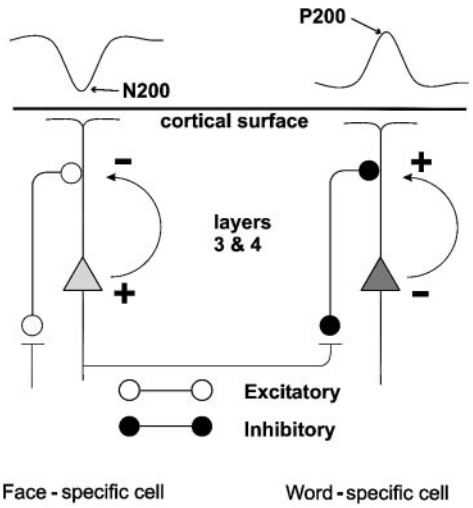

FIG. 3. Model of electrogenesis of N200 and P200 ERPs. N200 is the surface recording of excitatory depolarization of apical dendrites of layer 3 and 4 pyramidal cells. P200 is the surface recording of inhibitory hyperpolarization of apical dendrites due to recurrent collateral (illustrated) or another form of lateral inhibition. Current flows shown are extracellular and generate ERPs by synchronous excitation or inhibition of populations of such cells.

scenario, a patch of face-specific cells (for example) would send inhibitory projections to a nearby patch of word-specific cells. This would imply an afferent, bottom-up mechanism. The spotty electrode coverage over human inferior cortex precludes systematic measurement of distances between category-specific patches of cortex, but distances as small as 5 mm have been found (Puce et al. 1999, Fig. 8). Whether recurrent collateral inhibition or another form of lateral inhibition extends over (at least) 5 mm in human extrastriate cortex is unknown, but in cat, V1 horizontal connections can extend over 4 mm (Gilbert and Wiesel 1983). As demonstrated in Fig. 1, *A* and *B*, many face- and word-specific N200 sites do not generate P200s to nonpreferred stimuli. If recurrent collateral inhibition is localized, a given patch of category-specific cortex may receive little or no inhibitory input from distant patches of different specificity.

A rapid top-down inhibition from distant structures is also a possible generator of P200. Hupé et al. (2001) found in monkeys that feedback effects from area MT to areas V1-V3 often occurred within 10 ms of the initial feedforward activation and that inhibitory feedback was especially rapid. In favor of this idea is that feedback connections are likely to be primarily on the distal apical dendrites of layer 1 (Rockland 1997), where an inhibitory hyperpolarization would generate a strong surface-positive ERP (in this case the inhibition would be even more distal on dendrites than is illustrated in Fig. 3 for the cell on the right). P200 latencies that were consistently later than their corresponding N200s would be consistent with a distant inhibitory feedback. However, it can be calculated from the plots of Fig. 2*A* that at face-specific sites, P200s are on average only 1.1 ms later than their N200s; the corresponding value at word-specific sites is 3.2 ms. These delays seem to be too short for a distant feedback inhibition, even invoking the rapid inhibitory feedback described by Hupé et al. (2001). These considerations thus slightly favor the hypothesis of local feedforward inhibition as illustrated in Fig. 3.

This study focused on reciprocal face and word inhibition because the largest P200s were recorded to these two classes of stimuli, but the data of Fig. 1, *E* and *F*, and Fig. 2, *B* and *C*, suggest that between-category inhibition is a more general phenomenon. Category-sensitive inhibition may be a general feature of the operation of the human ventral object-recognition system. It may serve to suppress activity of nonpreferred cells and would thus act as a higher level "sharpening" mechanism analogous to the action of surround inhibition of cells in earlier stages of visual processing (Nicholls et al. 1992). However, this inhibition may not be as specific as its associated excitation; while the largest P200s were evoked by faces (at word-specific sites) and words (at face-specific sites), the next-largest P200s were evoked by the scrambled versions of these stimuli (Fig. 2, *B* and *C*). These results suggest that the category-sensitive inhibitory mechanism is somewhat "fooled" by the low-level features of faces and words.

Of the category-specific N200s, those selective for faces and words are by far the most common (Allison et al. 1999). This is perhaps not surprising, because these stimuli are particularly important for literate humans. The amount of cortex devoted to processing these two types of images is probably large, and thus the probability of recording their mutual inhibition may be correspondingly large. Alternatively, Farah (1994) proposed that object recognition needs only two processes, a holistic process required for faces (and useful for other objects) and a feature-based process required for words (and useful for other objects). It is possible that our results reflect the operation of these two subsystems—which we infer to be reciprocally inhibitory—rather than the operation of face and word subsystems per se.

In monkey inferotemporal cortex, local inhibition increases cell selectivity, while removal of inhibition decreases selectivity (Wang et al. 2000). The inhibition inferred in human inferotemporal cortex may serve a similar function. Faces generated P200s at word-specific sites that were on average twice as large as the P200 generated by words at face-specific sites, implying that the increased selectivity conferred by the proposed inhibition is more useful for face processing (perhaps because this homogeneous category of stimuli requires rapid and accurate processing) than for other categories of stimuli. In this regard, it is interesting that cells in the human hippocampus are much more likely to be inhibited by faces than by objects (Fried et al. 2002), suggesting that faces are a potent inhibitory stimulus at mnemonic as well as perceptual levels of object processing. In this study, faces and words were presented in isolation. In real world scenes, it is possible that face-specific cells (for example) inhibit word-specific cells primarily when attention is directed to faces, or it may be an automatic process regardless of the focus of attention. Studies to test these alternatives remain to be carried out.

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